EXHIBIT G

Information about Nitrosamine Impurities in Medications

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Latest Information

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Metformin (/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-metformin)

Ranitidine (Zantac) (/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine)

Rifampin/Rifapentine (/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-nitrosamines-rifampin-and-rifapentine)

Varenicline (Chantix) (/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-nitrosamine-varenicline-chantix)

What You Should Know about Nitrosamine Impurities

FDA issues guidance,"Control of N-Nitrosamine Impurities in Human Drugs"

Update [2/24/2021] To ensure the safety of the U.S. drug supply, the guidance recommends that manufacturers should conclude the risk assessment of approved or marketed products, the first of three steps manufacturers should follow to mitigate nitrosamine impurities in their products, within 6 months of publication of the guidance. Through today's revision to the guidance, FDA extends the recommended timeframe for completion of risk assessments to March 31, 2021. Manufacturers do not need to submit risk assessment documents to the agency, but they should retain these documents so that they are available if requested.
[9/1/2020] FDA is announcing the availability of a guidance for industry, entitled "Control of N-Nitrosamine Impurities in Human Drugs (/regulatory-information/search-fda-guidance-documents/control-nitrosamine-impurities-human-drugs)." This guidance recommends steps manufacturers of active pharmaceutical ingredients and drug products should take to detect and prevent objectionable levels of nitrosamine impurities in pharmaceutical products. The guidance also describes conditions that may introduce nitrosamine impurities.

What patients should know about nitrosamine impurities

- FDA has been investigating the presence of impurities, called nitrosamines, in some types of medications.
- Nitrosamines are common in water and foods, including cured and grilled meats, dairy products and vegetables. Everyone is exposed to some level of nitrosamines.
- FDA, in collaboration with regulatory counterparts around the world, has set internationally-recognized acceptable daily intake limits for nitrosamines. If drugs contain levels of nitrosamines above the acceptable daily intake limits, FDA recommends these drugs be recalled by the manufacturer as appropriate.
- Nitrosamine impurities may increase the risk of cancer if people are exposed to them above acceptable levels and over long periods of time, but a person taking a drug that contains nitrosamines at-or-below the acceptable daily intake limits every day for 70 years is not expected to have an increased risk of cancer.
- Patients taking prescription medications with potential nitrosamine impurities should not stop taking their medications. Patients should talk to their health care professionals about concerns and other treatment options.
- Consumers taking over-the-counter medications with potential nitrosamine impurities may consider using other OTC products approved for their condition.

- Find information about medications that have been recalled due to potential nitrosamine impurities on the FDA recalls webpage (/safety/recalls-market-withdrawals-safety-alerts).
- The agency is working to determine the source of these impurities and will keep the public informed.

What health care professionals should know about nitrosamine impurities

- Health care professionals should continue to prescribe medications when clinically appropriate even though they may have low levels of nitrosamine impurities.
- Health care professionals can educate patients about alternative treatment options to medications with potential nitrosamine impurities if available and clinically appropriate.
- Find information about medications that have been recalled due to potential nitrosamine impurities on the FDA recalls webpage (/safety/recalls-market-withdrawals-safety-alerts). (https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/mylan-initiates-voluntary-nationwide-recall-three-lots-nizatidine-capsules-usp-due-detection-trace)
- If a medication has been recalled, pharmacists may be able to dispense the same medication from a manufacturing lot that has not been recalled. Prescribers may also determine whether there is an alternative treatment option for patients.
- FDA will continue to investigate the presence of nitrosamine impurities in drugs and will communicate new information as it becomes available.

What industry should know about nitrosamine impurities

- Manufacturers are responsible for understanding their processes, which includes preventing the presence of unacceptable impurities. Manufacturers are also responsible for developing and using suitable methods to detect and limit unacceptable impurities, including any new impurities that may arise when they make changes to their manufacturing processes.
- FDA has published testing methods that can be used by industry to detect nitrosamine impurities.
- FDA, in collaboration with regulatory counterparts around the world, has set internationally-recognized acceptable daily intake limits for nitrosamines. If drugs contain levels of nitrosamines above the acceptable daily intake limits, FDA recommends these drugs be recalled by the manufacturer as appropriate or not be released for distribution to the market.
- The agency is working with industry to determine the source of these impurities, but there are multiple reasons why nitrosamines can be present in medicines.

Why are some drugs being recalled due to a potential nitrosamine impurity while others are not?

FDA, in collaboration with regulatory counterparts around the world, has set internationally-recognized acceptable daily intake limits for nitrosamines. Nitrosamines below this level are acceptable in drugs. If drugs contain levels of nitrosamines above the acceptable daily intake limit, FDA recommends these drugs be recalled by the manufacturer.

Some manufacturers have recalled certain drugs as a precautionary measure, while others have been recalled after testing positive for nitrosamine levels above the acceptable daily intake limits. Information about drugs that have been recalled due to potential nitrosamine impurities can be found on the FDA recalls webpage (/safety/recalls-market-withdrawals-safety-alerts/mylan-initiates-voluntary-nationwide-recall-three-lots-nizatidine-capsules-usp-due-detection-trace).

What is the risk of taking a drug that contains nitrosamines?

FDA does not expect nitrosamines to cause harm when ingested at low levels. Nitrosamine impurities may increase the risk of cancer if people are exposed to them above acceptable levels and over long periods of time, but a person taking a drug that contains nitrosamines at, or below, the acceptable daily intake limits every day for 70 years is not expected to have an increased risk of cancer.

Why are nitrosamine impurities present in drugs?

There are multiple reasons why nitrosamines can be present in drugs. FDA found the source of nitrosamines can be related to the drug's manufacturing process or its chemical structure or even the conditions in which they are stored or packaged. As foods and drugs are processed in the body, nitrosamines can also be formed. FDA continues to test and research possible sources for drugs found to contain nitrosamines.

Is the presence of nitrosamines in drugs a new problem? Why have there been so many recent reports of drugs containing nitrosamines?

FDA has ongoing assessment, surveillance, compliance and pharmaceutical quality efforts across every product area, and we will continue to work with drug manufacturers to ensure safe, effective and high-quality drugs for the American public. When we identify new and previously unrecognized risks to safety and quality, we react swiftly to resolve the problem, as we have done in responding to the recent findings of nitrosamines in certain medicines.

Today, we have better testing methods than ever before, and we know what to look for in products' chemical structures and manufacturing processes that may increase the risk of forming low levels of nitrosamines. Improved technology enables us to detect even trace amounts of impurities in drug products and may be the reason why more products have been found to have low levels of nitrosamines. The agency has strict standards for safety, effectiveness and quality, and our staff makes every effort to help keep the U.S. drug supply as safe as possible. We also work closely with international drug regulatory agencies so that we leverage resources and testing done outside the U.S.

which can help inform testing of the U.S. drug supply. As our investigations and testing continues, along with the investigations done by other drug regulatory agencies, we may find low levels of nitrosamines in additional drugs.

Can we trust FDA and its approvals and drug surveillance?

FDA is committed to ensuring that the medicines Americans take are safe and effective. We continually gain new knowledge about drugs which allows us to identify and quickly address previously unknown risks to patients. When we identify drug quality lapses that pose potential risks for patients, we make every effort to understand the issues and provide our best recommendation to the public as quickly and accurately as possible. We will continue to investigate and work to ensure these types of impurities do not exceed acceptable limits so that patients can continue taking their medicines without concern.

Resources for You

- Stakeholder Questions for May 4th FDA-Industry Meeting to Discuss Nitrosamine Impurities in Pharmaceuticals (/media/150864/download)
- Video: A Message for Patients about ARBs (https://youtu.be/BLZMnHxyfqg) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) | Transcript (/drugs/drug-safety-and-availability/transcript-angiotensin-ii-receptor-blockers-arbs-message-patients)
- FDA Recalls – Recalls, Market Withdrawals, & Safety Alerts (/safety/recalls-market-withdrawals-safety-alerts)
- What to Know and Do About Possible Nitrosamines in Your Medication (/consumers/consumer-updates/what-know-and-do-about-possible-nitrosamines-your-medication)